REMARKS/ARGUMENTS

Claims 1-125 were in the application as originally filed. Claims 2-5, 7, 8, 10-11, 20, 26-30, 33-34, 40-51, 53-59, 61-64, 67-69, 73-75, 77-79, 81-83, 85-87, 89-91, 93-123 have been canceled. Cancellation of claims in this response is done without prejudice to, or disclaimer of, the subject matter therein. New claim 126 has been added by the present amendment.

Claims 1, 6, 9, 12-19, 21-25, 31-32, 35-39, 52, 60, 65-66, 70-72, 76, 80, 84, 88, 92, 124-125 are now pending after the cancellations made herein. All of these remaining claims have been rejected in their earlier form.

Further examination and reconsideration of this application is respectfully requested in view of the foregoing amendments and the following remarks.

A. Objections to Claims

Claims 19, 21-25, 31-32, 35-39, and 92 were objected to because of the abbreviations "MRI" in claims 19, 37, and 92 and "PET" in claim 19 (and, thereby, in its dependent claims 21-25, 31-32, and 35-39). The claims have been amended to provide the full names: magnetic resonance imaging (MRI) and positron emission tomography (PET) upon their first occurrence in the claim set, and, thereafter, the abbreviations are used.

B. The Specification

The Office Action notes use of trademarks in the application without capital letters or, as an alternative, use of generic terminology. The specification and claims have been amended to capitalize all of the trademarks used.

The Office Action also notes the absence of any Abstract page. A separate Abstract page has been filed concurrently with this amendment.

C. Claim Rejections - 35 U.S.C. § 112, Second Paragraph:

Claims 1, 4, 6, 7, 9, 12-19, 21-25, 31-32, 35-39, 45-47, 49-52, 58-60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite due to recitation of the term "derivative" in a number of these claims. The claims have been amended so that the term "derivative" no longer appears in any of the claims. This ground for rejection may therefore be withdrawn.

The Office Action asserts that claims 4 and 6 are indefinite for use of the language "biological or structural characteristics" and that claim 6 is also indefinite for use of "corresponding regions or sites". Although Applicants disagree with these grounds for rejection, to advance prosecution, claim 4 has been canceled and claim 6 amended to delete this specific language. This basis for rejection may therefore be withdrawn.

Claims 6, 7, 12, 17, 45-47, 49-52, 58-60, 65-66, 70-72, 76, 80, 84, 88, and 92 were rejected as indefinite for reciting the term "Met". These claims have been amended by specifying that "Met" refers to "receptor protein tyrosine kinase Met"(see, specification at page 2, line 16).

D. Claim Rejections - 35 U.S.C. § 112, First Paragraph, Deposit:

Claims 1, 4, 6, 7, 9, 12-19, 21-25, 31-32, 35-39, 45-47, 49-52, 58-60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. More specifically, the Office Action indicated that certain identifying information for the deposits should be added to the specification. The specification has been amended

to add the requested information (see, paragraph 00115). Also, the Office Action required statements regarding the irrevocability of the deposits pursuant to 37 CFR 1.803-1.809. Attached as Exhibit A are the signed applications/statements made by one of the inventors as part of the ATCC deposit process for mAbs Met3 and Met5, along with the ATCC deposit receipts. With respect to the mAbs for HGF (A.1, A.5, A.7, and A.10), it is believed that one of the inventors also must have made the required statement under the Budapest Treaty because an ATCC receipt for these HGF mAbs also was issued. (The ATCC receipt for the HGF mAbs is attached as part of Exhibit A.) Although the signed application/statement for the ATCC deposit process for mAbs for HGF is unavailable, Applicants respectfully submit the requirement also has been met for these mAbs.

E. Claim Rejections - 35 U.S.C. § 112, First Paragraph, Written Description:

Claims 1, 6, 9, 12-19, 21-25, 31-32, 35-39, 52, 60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 stand rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the written description requirement (Office Action, pp. 6-11). More specifically, the Office Action indicates that the specification "does not disclose the specific structure of the epitope of the claimed monoclonal antibody" and

> "...it is not clear that the epitope of the claimed monoclonal antibody is the extracellular domain of which variant Met protein, because the specification does not disclose the extracellular domain of a specific Met protein identified by a sequence identification number, and because Met protein encompasses a genus of variant Met with different or unknown structure."

(Office Action, pp. 6-7).

First, Applicants wish to seek clarification of the language of the Office Action. Applicants assume that the intent was not to refer to "epitopes of the mAb", but rather on epitopes bound or recognized by the monoclonal antibody (hereinafter abbreviated as "mAb") on the "antigen", namely epitopes of Met (or in the case of claims 13 and 14, epitopes of HGF).

Claim 1 (as examined and as amended) is directed to mAbs Met3 and Met5 produced by the hybridoma cell lines deposited in the ATCC and granted Accession Numbers PTA-4349 and PTA-4477, respectively, and their antigen binding fragments. New claim 126 specifically defines several particular types of these fragments. No reference is made to "derivatives" of the mAbs in any of the pending claims. Applicants respectfully submit that the human Met epitope recognized by the claimed mAbs cannot be considered a genus of Met variants. The epitope bound by each of these claimed mAbs is inherent to the mAb due to the structure of its antigen-binding region(s) (such as the V regions, the CDR's , *etc.*, as is well-known in the art). Accordingly, Applicants respectfully submit that a person of ordinary skill in the art would understand that at the time the application was filed Applicants were in possession of the invention defined by amended claim 1-- the two mAbs and their antigen-binding fragments.

The same can be said of inventions defined in the claims dependent from claim 1. Claims 6, 9, 12-19, 21-25, 31-32, 35-39, 52, 60, 65-66, 70-72, 76, 80, 84, 88 and 92, each include features described in the application in addition to the features of the mAbs themselves. Claims 124 and 125 are directed to the hybridoma cell lines deposited in the ATCC and granted Accession Numbers PTA-4349 and PTA-4477 which produce Met3 and Met5, respectively. Accordingly, Applicants respectfully submit the invention claimed in present claims 1, 6, 9, 12-19, 21-25, 31-32, 35-39, 52, 60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 is described in the application in a way that fully complies with the Written Description requirement of § 112.

F. Claim Rejections - 35 U.S.C. § 112, First Paragraph, Enablement:

Claims 1, 6, 9, 12-19, 21-25, 31-32, 35-39, 52, 60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 stand rejected under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the enablement requirement.

The Office Action asserts that adequate support for claims 1, 4, 6, 7, 9, 12-19, 21-25, 31-32, 35-39, 45-47, 49-52, 58-60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 depends upon certain "essential material" that is provided only by incorporation by reference of foreign patent documents or non-patent documents. The Office Action states that Applicants must introduce the Met and HGF sequences cited in the published reference referred to in the specification, along with Sequence Listings and the required accompanying statements (that paper and CRF listings are the same, that no new matter is added, and that the amendatory material consists of the same material incorporated by reference). Applicants disagree with this position as it would apply to the present claims, because none of the pending claims recite "epitopes" in the way that prior claim 7 did. Canceled claim 7 recited:

> *A human monoclonal antibody specific for Met that binds to the same **epitope** as the **epitope** to which the monoclonal antibody of claim 1 binds...*

However, to advance prosecution, Applicants nevertheless are adding a Sequence Listing to the application (along with the following statement) and are amending the specification to identify the amino acid and cDNA sequences for human Met, human HGF, and the ECD of human Met (SEQ. ID NOS:1-5).

STATEMENT IN SUPPORT OF SEQUENCE LISTING REQUIREMENTS

[0001] I hereby state that: in accordance with 37 C.F.R. 1.821(f), that the content of the attached computer readable copy of the sequence listing and the paper copy are believed to be the same, and,

in accordance with 37 C.F.R. 1.821(g), the submission is not believed to include new matter. Furthermore, the Sequences described in the Sequence Listing (of human Met and human HGF) are the subject of a number of the documents incorporated by reference in the specification and were known to those of skill in the art at the time the invention was made and at the time the application was filed. The text file filed concurrently with this application, titled "Sequence_Listing.txt" contains material identified as SEQ ID NO: 1-5, which material is incorporated herein by reference. This text file was created on October 30, 2007, and is 37,065 bytes.

Claims 1, 4, 6, 7, 9, 12-19, 21-25, 31-32, 35-39, 45-47, 49-52, 58-60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 were also rejected as failing to comply with the enablement requirement based on the presence of certain language described below:

(a) a *derivative* of a mAb and a method for detecting Met using this derivative (claims 1, 4, 6, 7, 9, 12-19, 21-25, 31-32, 35-39, 45-47, 49-52, 58-60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125);

(b) a mAb allegedly specific for a "*genus of Met variant*" (claims 6, 7, 9, 12-14, 17-18, 45-47, 49-52, 58-60, 65-66, 70-72, 76, 80, 84, 88, and 92);

(c) a mAb useful for *treating* a tumor allegedly expressing a *genus of Met variant* (claims 45-47, 49-52, 58-60, and 65);

(d) a method of detecting the presence of an alleged *genus of Met variant* using the claimed mAb (claims 66, 70-72, 80, 84, 88, and 92); and

(e) a mAb allegedly specific for a *genus of HGF variant* (claims 13 and 14).

With respect to item (a) above ("derivative" language), as noted above, this term has been deleted from all remaining claims where it previously was found.

With respect to items (b)-(e) above, the Office Action alleges that because one cannot predict that the claimed mAb would be useful for detecting or treating cancer, one would not know *how to use*

the claimed mAbs (Office Action, p. 14). The Office admits that Applicants taught the use of the claimed mAbs for the detection of Met in tumor tissue, citing Examples 4 and 5.

Further, the Office asserts that a person of skill in the art would not know how to use the claimed mAbs because the expression of Met variants or HGF variants in cancer tissue is unpredictable as such expression may differ from that in normal tissue (Office Action, pp. 14-15). The Office Action also states that because one cannot predict that variant Met or HGF proteins are expressed or overexpressed in cancer tissue, one cannot predict that the claimed antibodies can be used to detect cancer (Office Action, pp. 14-15).

As noted above, the specification teaches use of the claimed mAbs to detect Met in tumor tissue (see, Examples 4 and 5). Moreover, as set forth in the application, aberrant expression of Met and HGF is involved in numerous types of solid tumors, and mutations in Met have been shown to contribute to a variety of human cancers (see, application paragraphs 006-009).

Applicants believe that the present amendments, if still deemed necessary, are sufficient to put to rest the above basis for rejection, so that the rejection may be withdrawn.

The Office also appears to be particularly concerned that claims 1, 4, 6, 7, 9, 12-19, 21-25, 31-32, 35-39, 45-47, 49-52, 58-60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 lack enablement because there is no disclosure of the structure of the epitope *of* [*sic*: recognized by] the claimed mAb, such as a "specific extra-cellular domain" of Met that should be identified by a sequence identification number (Office Action, p. 13). As noted above, the specification has been amended to include explicitly the well-known sequence of the human Met ECD (SEQ ID NO. 3). Although, as discussed above, Applicants believe they should not be required to identify any "specific epitope" in structural terms in view of their amendments and cancellations of the relevant claims.

Claims 45-47, 49-52, 58-60, and 65 also allegedly lack enablement because, according to the Office, one cannot predict that the claimed mAbs could be used to treat cancer; stated otherwise, Applicants have presented no data that these antibodies are antagonists of Met while "immunotherapies are unpredictable" (Office Action, pp. 15-17). The Examiner's attention is respectfully drawn to the fact that none of the remaining claims in this rejected group recite "therapy", or use the term "therapeutic composition." Therefore, this basis for rejection is now moot.

Claim 65 was rejected as lacking enablement allegedly because one cannot predict that the claimed mAbs could be used for prognosis of cancer. The Office takes this position because Applicants allegedly do not teach how to correlate the claimed mAbs with determining the risk of cancer (Office Action, pp. 17-19). Claim 65 has been amended to delete the terms "prognose" and "prognosing", thereby rendering moot this basis for the above rejection.

Another reason for the rejection of claims 45-47, 49-52, 58-60, and 65 was said to be the presence of the word "tumor". The Office Action alleges that this term encompasses tumor cells that may not be cancerous (Office Action, pp. 19-20). While Applicants disagree with this analysis as being merely "form over substance", they have nevertheless amended claims 52, 60, and 65 (which no longer recite "tumor") and have canceled claims 45-47, 49-51, 58, and 59.

Applicants respectfully submit that in view of the above amendments and remarks, claims 1, 6, 9, 12-19, 21-25, 31-32, 35-39, 52, 60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 meet the enablement requirements of the statute because one of ordinary skill could make and use the invention as now claimed without undue experimentation. Based on the foregoing, Applicants respectfully request withdrawal of the Section 112 rejection of claims 1, 6, 9, 12-19, 21-25, 31-32, 35-39, 52, 60, 65-66, 70-72, 76, 80, 84, 88, 92, and 124-125 and allowance of these claims.

G. Claim Rejections - 35 U.S.C. § 102:

Claims 1, 6, and 9 were rejected under 35 U.S. C. § 102 as being anticipated by Prat et al., 1991, Mol. Cell Biol. 11 (12):5954-5962 (hereinafter "Prat"). The Office Action indicates that Prat seems to disclose either (a) a derivative or (b) a mAb having all of the identifying biological characteristics of the mAb of claim 1 (Office Action, p. 22). As already discussed, Applicants have amended claims 1, 6, and 9 to delete the term "derivative," and claims 4 and 6 have been canceled. Accordingly, mAbs that allegedly have the characteristics of those disclosed by Prat are no longer claimed. Likewise, Prat does not, and by its terms cannot, disclose the specific mAbs Met3 and Met5. For this reason, Applicants respectfully submit that the Section 102 rejection should be withdrawn and the present claims deemed free of the prior art.

Conclusion

For the reasons discussed above, all claims now pending in the application comply with §112 with respect to definiteness and support under the Written Description and Enablement requirements, and are free of the cited prior art. Thus, these claims are allowable. Early notification of such allowability is respectfully requested.

If there are any outstanding issues which the Examiner feels may be resolved by way of telephone discussions, the Examiner is cordially invited to contact the undersigned at the telephone number shown below.

Respectfully submitted,

October 30, 2007
Date

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